

Application No. 09/724,961
Amendment dated August 18, 2003
Reply to Office Action mailed May 16, 2003

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Amendments to the Specification:

Please replace the "cross-reference to related applications" section with the following replacement section:

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This application is a continuation of U.S. Application No. 09/580,015 filed May 26, 2000, which is a continuation-in-part of U.S. Application No. 322,289, filed May 28, 1999, which is a continuation-in-part of U.S. Application No. 09/201,430, filed November 30, 1998, which is an application claiming the benefit under 35 U.S.C. 119(e) of U.S. Application Nos. 60/080,970, filed April 7, 1998, and 60/067,740, filed December 2, 1997. Each of the above applications is incorporated herein by reference.

~~This application is a continuation in part of USSN 09/322,289, filed May 28, 1999, which is incorporated by reference in its entirety for all purposes. This application is also a continuation in part of PCT/US98/25386, filed November 30, 1998, and USSN 09/201,430, filed November 30, 1998, both of which claim priority from USSN 60/080,970, filed April 7, 1998, and USSN 60/067,740, filed December 2, 1997. Each of the above applications and Townsend and Townsend and Crew Attorney Docket 015270-004750PC, filed May 26, 2000, is incorporated by reference in its entirety for all purposes.~~

Please replace the paragraph beginning on page 7, line 12 of the specification with the following replacement paragraph.

Fig. 10: Lymphocyte Proliferation Assay on spleen cells from AN1792-treated (Fig. 10A)(upper panel) or PBS-treated (Fig. 10B)(lower panel).

et al., *J. Mol. Biol.* 215:403-410 (1990). Software for performing BLAST analyses is publicly available through the National Center for Biotechnology Information

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(~~http://www.ncbi.nlm.nih.gov/~~) Typically, default program parameters can be used to perform the sequence comparison, although customized parameters can also be used. For amino acid sequences, the BLASTP program uses as defaults a wordlength (W) of 3, an expectation (E) of 10, and the BLOSUM62 scoring matrix (see Henikoff & Henikoff, *Proc. Natl. Acad. Sci. USA* 89, 10915 (1989))

For purposes of classifying amino acids substitutions as conservative or nonconservative, amino acids are grouped as follows: Group I (hydrophobic sidechains): norleucine, met, ala, val, leu, ile; Group II (neutral hydrophilic side chains): cys, ser, thr; Group III (acidic side chains): asp, glu; Group IV (basic side chains): asn, gln, his, lys, arg; Group V (residues influencing chain orientation): gly, pro; and Group VI (aromatic side chains): trp, tyr, phe. Conservative substitutions involve substitutions between amino acids in the same class. Non-conservative substitutions constitute exchanging a member of one of these classes for a member of another.

Therapeutic agents of the invention are typically substantially pure from undesired contaminant. This means that an agent is typically at least about 50% w/w (weight/weight) purity, as well as being substantially free from interfering proteins and contaminants. Sometimes the agents are at least about 80% w/w and, more preferably at least 90 or about 95% w/w purity. However, using conventional protein purification techniques, homogeneous peptides of at least 99% w/w can be obtained.

Specific binding between two entities means an affinity of at least 10^6 , 10^7 , 10^8 , 10^9 M⁻¹, or 10^{10} M⁻¹. Affinities greater than 10^8 M⁻¹ are preferred.

The term "antibody" or "immunoglobulin" is used to include intact antibodies and binding fragments thereof. Typically, fragments compete with the intact antibody from which they were derived for specific binding to an antigen fragment including separate heavy chains, light chains Fab, Fab' F(ab')₂, Fabc, and Fv. Fragments are produced by recombinant DNA techniques, or by enzymatic or chemical separation of intact immunoglobulins. The term "antibody" also includes one or more immunoglobulin chains that are chemically conjugated to, or expressed as, fusion proteins with other proteins. The term "antibody" also includes bispecific antibody. A bispecific or bifunctional antibody is an artificial hybrid antibody having two different heavy/light chain pairs and two different binding sites. Bispecific antibodies can be produced by a variety of methods including fusion of hybridomas or linking of Fab' fragments. See,